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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,271	06/28/2006	Helena Edlund	1501-1319	3105

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EXAMINER
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ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,271	EDLUND ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

Priority date for elected invention is applied under 35 USC§119(e) for the provisional Application No.60/481, 249 filed on 08/18/2003.

The abstract is objected because the as-filed application does not contain a separate sheet disclosing only the abstract.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 10-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse over-expressing GPR40 comprising the promoter Ipf1/Pdx1 and a method of its use, does not enable any transgenic non-human laboratory animal over-expressing GPR40 or their use thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At issue, under the enablement requirement of 35 U.S.C. 112, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170

USPQ 276 (CCPA 1970). These factors include, but are not limited to: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the prior art; (4) The level of one of ordinary skill; (5) The level of predictability in the art; (6) The amount of direction provided by the inventor; (7) The existence of working examples; and (8) The quantity of experimentation needed to make or use the invention based of the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). All of the wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below as to show that one of the ordinary skill in the art have to go through "undue experimentation" in order to practice the invention.

Nature of the invention: The invention relates to generation of transgenic laboratory animals over-expressing GPR40 comprising the promoter Ipf1/Pdx1 with Type-II diabetes and a method oft their use.

Breadth of the claims And Guidance Provided in the Specification: The of invention as claimed encompasses any transgenic laboratory animals (insects, rabbits, fish, earthworms, mollusks, monkeys etc) over-expressing GPR40 transgene comprising the promoter Ipf1/Pdx1 with Type-II diabetes and a method oft their use.

At the best specification teaches a transgenic mouse over-expressing GPR40 transgene comprising the promoter Ipf1/Pdx1 with Type-II diabetes and a method oft their use for screening compounds for GPR40 modulation.

The specification does not teach any other laboratory animal or animals or sufficient number of examples of laboratory animals that over-express GPR40 transgene and exhibit Type II diabetes phenotype.

In the absence of representative number of enabled examples in the specification commensurate with the breadth of the claims one of ordinary skill in the art would conclude that the invention is unpredictable and would require undue experimentation to practice the invention in its full scope. Applicants' attention is drawn to In re Shokal, 242 F.2d 771,, 113 USPQ 283 (CCPA 1957). The test is whether the number of claimed genus/or species of laboratory animals are transgenic for over-expression of GPR40 and exhibiting Type II diabetes phenotype are successfully completed by applicants as

instantly claimed and prior to the reference date or the date of the activity provided an adequate basis for inferring that the invention has generic applicability.

The level of one of ordinary skill in the Art at the Time of Invention: The level of one of ordinary skill in the art at the time of filing of the instant application is high requiring an advanced degree or training in the relevant field. The status of the art at the time of filing was such that said skilled in the art would not have been able to make or use the invention for its fully claimed scope without undue experimentation.

State of the Art, the Predictability of the Art: At about the effective filing date of the present application art is unpredictable with regard to There still exists unpredictability in the art regarding both structure/function prediction of the mutated or engineered proteins as well as to what phenotype/s they may lead to in transgenic cell or the transgenic/recombinant animal models including mice. Note that the mere capability to perform gene transfer in a mouse is not enabling because a desired phenotype of over-expressing GPR40 transgene over normal controls for example cannot be predictably achieved by simply introducing a vector constructs with a GPR40 transgene as broadly claimed. Further, given the paucity of information in the relevant art, one of ordinary skill in the art would not be able to predict the phenotype of a transgenic non-human animal bearing over-expressing GPR40 transgene. Bockamp et al. Physiol. Genomics 11:115-132, 2001, state that "In experimental settings, use of conventional transgenic technology control over the onset of transgene expression will strictly depend on positional integration effects and on the nature of the chosen regulatory elements. However, constitutive expression of a transgene is often too inflexible to meet the needs of a specific experimental question. For example, too early or too widespread expression of the transgene may lead to phenotypic or physiological aberrations producing secondary pleiotropic responses as a result of the introduced genetic alteration. Distinguishing effects of the resulting phenotype might turn out to be extremely difficult, as cell autonomous versus cell non-autonomous effects are not clearly divisible and compensatory systemic changes are often concealed".

Regarding transgenic animals the unpredictability of phenotypes of transgenic animals in conventional transgene introduction arises due to transgene random integration

into the host genome and subsequent aberrations namely poor expression, temporally and/or spatially aberrant expression, position effects etc., (Bishop Reproductive Nutrition and Development 36: 607-616, 1996; p.614 1st col. 3rd pg. & 2nd col. 1st¶). Further unpredictability arises owing to the functional and physiological effects of the expressed transgene (foreign gene), interference of the redundant native genes, induction of compensatory processes, gene silencing effects as well as due to the influence of genetic background and the phenomenon of imprinting (reviewed in Rulicke and Hubischer, Experimental Physiology 85: 589-601, 2000; p.595 1st col. 1st ¶). Holschneider et al. Int J. Devl. Neuroscience 18:615-618, 2001, discuss various factors that contribute to the resulting phenotype of transgenic mice, including compensatory systems which may be activated to mask the resulting phenotype, these compensatory changes may be due to the differential expression of another gene. "The use of conditional and inducible transgenic systems can permit the study of a phenotype containing or lacking the transgene product at any given developmental stage of the same individual. This could enable experimental approaches that can either focus on specific time points or in specific tissues during development, on effects of the duration of transgene expression and on the reversibility of induced phenotypes" (Rulicke & Hubischer, Experimental Physiology 85: 589-601, 2000; se p. 597, 1st col., 4th ¶).

Amount of experimentation necessary: Because of the lack of working examples, insufficient guidance and direction provided by Applicant, the inherent unpredictability of the art, and the nature of the invention, one of skill in the art would be required to perform a large amount of experimentation to make and/or use the invention in its full scope as claimed by Applicant. Such experimentation would be required to identify sufficient number of different laboratory animals and generate over-expressing GPR40 transgene. One of ordinary skill further use the said identified mutants above to generate transgenic or recombinant animals that possess the property of exhibiting Type II diabetes phenotype as laboratory animals of various animals used in research institutions and industries differ widely in their metabolic controls. Accordingly, in view of the lack of teachings in the art and lack of guidance provided by the specification with regard to sufficient number laboratory animals over-expressing GPR40 transgene and exhibiting

Type II diabetes phenotype as of around the filing date of instant application and for the specific reasons cited above, it would have required undue experimentation for one of skill in the art to make and use the full scope of the claimed invention. At the best the specification as filed is found only enabled for a transgenic mouse over-expressing GPR40 transgene comprising the promoter Ipf1/Pdx1 with Type-II diabetes.

The phenotype and the asserted use of transgenic animal is critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188, USPQ 356 (CCPA 1976). The applicant can over come this rejection by including the phenotype and the use of claimed transgenic non-human animal in the main claim (Clm 10).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 10-18 are rejected under 35 USC 102 (e) as being anticipated by Hinuma et al., (Patent Pub No: US2005/0089866 A1).

The above claims are directed to a transgenic non-human animal over-expressing GPR40 comprising Ipf1/pdx1 promoter controlling the expression of GPR40 wherein the animal is a mouse or rat and to a method of testing compounds possessing certain effect for treating diabetes Type 2

Regarding claims 10-12 Hinuma teaches a transgenic mouse or a rat in which an exogenously introduced GPR40 gene is over-expressed under the control of any mammalian promoter thus encompassing Ipf1/Pdx1 promoter (p.40, paragraphs 068-0615, p.41 paragraphs 0616-0618 and 0621-0626 and claims 1, 93-95). Regarding claim 13-18 Hinuma teaches the use of normal GPR40 over-expressing transgenic non-

human animal can be utilized as a pathologic model animal for such a disease and said animal is usable for screening of an drug for treatment of diseases associated with the over-expression GPR40 that include for example type II diabetes mellitus, obesity, hyperlipidemia and others (p.27, paragraphs 0411-0412; p.42, paragraph 0632-0633) and further the method provides methods of screening compounds that changes the expression level of GPR40 (p.27, paragraphs 0412-0415, p.28 0423-0428) and the compounds obtained could be used for treating diseases including Type II diabetes (p.28, paragraphs 0425-0428; p.29 paragraphs 0435) and effects on the levels various metabolites in said animal (for example see p.35 paragraphs 0536-0539, p.37, paragraphs 0558-0561). The cited art thus anticipates the invention as claimed.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is ***571 272-0548.*** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

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